Melanoma: Diagnosis, Staging and Treatment

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The Bad Guy (Girl)
### Definition

- Malignant transformation of melanocytes
- Most melanocytes occur in skin at the epidermal/dermal junction but can also occur in the retina and certain neural tissue since the melanocyte is derived from the neural crest embryologically.

### Epidemiology

- Lifetime risk between 1 in 75-1 in 50
- 55,000 new cases of melanoma yearly in USA
- 5% of all new cancers in the USA
- 8,000 deaths per year and is the most fatal skin disease in the world
Risk Factors

- **Skin type**
  - Type 1: always burns never tans
  - Type 2: always burns and sometimes tans
  - Type 3: sometimes burns and always tans
  - Type 4: never burns and always tans
- **The correlation of eye color and freckling or phenotypes also relates to skin type and risk**

- **Sunlight exposure “Latitude gradient”**
  - The incidence of melanoma is inversely proportional to the latitude
  - If you live closer to the equator, you’re more likely to get melanoma
- **Occupation and socio-economic status**
  - May relate to sunlight exposure
Risk Factors – cont’d

- **Family history**
  - Melanoma more likely to occur if a positive family history

- **Gender and hormonal status**
  - Women generally have a more favorable prognosis of melanoma than men which may relate to female hormonal status.

Types of Melanoma

- **Superficial Spreading Melanoma**
  - Most common and represents 70% of all melanomas
  - Initially has a radial growth phase before evolving into a vertical growth phase
  - Depth determines prognosis
Superficial Spreading Melanoma

Superficial Spreading Melanoma
Types of Melanoma

- Nodular melanoma starts as a raised lesion and lacks the horizontal or lateral growth phase
- Occurrence 15-30% according to different studies
- Growth is much more rapid and consequently has a more guarded prognosis
Nodular Melanoma

Nodular Melanoma with Ulceration

Nodular Melanoma

1. Nodule with ulceration
2. Nodule with central scar
3. Asymmetry
4. Asymmetry
Types of Melanoma

- Lentigo Maligna Melanoma occurs 4-15% and as expected occurs almost exclusively on the head and the neck.

Lentigo Maligna Melanoma
Lentigo Maligna Melanoma

Types of Melanoma

- **Acral Lentiginous Melanoma**
  - Racial divide
  - Only 2-8% in fair skin whites
  - Represents the most common in African Americans – 60-72%
  - Occurs on palms and soles and subungal of the nail bed
Acral Lentiginous Melanoma

Spilling of pigment from the nail onto the skin which separates clinically from traumatic hemorrhage.
Diagnosis:

1. Clinical – Macroscopic
2. Dermoscopy
3. Consultation
   A. Specimen to Pathologist (Biopsy)
   B. Patient with specimen to Dermatologist for a clinical consultation

Clinical (Macroscopic)

- A – Assymetry
- B - Border (Irregular)
- C - Color changes
  - Variations of the American Flag Sign (Red, White and Blue)
- D - Diameter > 6mm
Clinical (Macroscopic) – cont’d

- **E - Evolving**
  - Looks different that it did before
  - Importance of photography with the advent of digital photography it has becomes less dependent on history
  - Can map out at risk patients or lesions with ease and store them in your computer for future evaluation.
  - Photography for documentation of existing lesions for location and observation for change
  - Nikon D 40 camera with a Macro lens which allows close-up examination of photos
  - Our office has switched to EMR (EHR) and we download the photos to each patient’s records to become a permanent part of the medical record

Clinical Evaluation

- **A. Asymmetry**
  - Symmetrical
  - Asymmetrical

- **B. Border**
  - Even edges
  - Uneven edges

- **C. Color**
  - One shade
  - Two or more shades

- **D. Diameter**
  - Smaller than 6 mm
  - Larger than 6 mm

- **E. Evolution**
Dermoscopy

- Clinical evaluation with enhanced epiluminescence (ELM)
  - Hand-held scope similar to an otoscope held against the lesion which magnifies 5x-10x with light on the pigmented lesion
  - Would represent an evaluation between gross vision and histology

Dermoscopy – cont’d

- Basic three parameters
  - Symmetry (Asymmetrical or Symmetrical)
  - Pigment pattern (Atypical or Typical)
  - Blue-White Structures

- Other Features
  - Brown globules (large brown dots in melanoma)
  - Pseudo pods sticks with dots at the ends
  - Depigmentation
Dermoscopy

Dermoscopy
Dermoscopy

Units Available

- Retail: DermLite® DL 100 – Cost: $275
- Reister ri-derma-dermatoscope® on Arial Medical Equipment site – Cost: $326
- Heine Delta 20 Dermatoscope (Delasco®) – Cost: $1,100
Dermoscopy – cont’d

- Many of these have photographic attachments to Nikon Coolpix and Sony Cyber-shot digital cameras to place your dermoscopy photos into your electronic records.
- Many of these companies retail attachments for the camera that can be attached to the dermoscopic instruments.
- All of this can be easily researched through that great medical search engine Google.

Reference Text

- Dermoscopy the Essentials by Robert Johr, et al (Mosby Publishers)
- Retails $72.00 on E-bay $66.43
Consultation

- Pathologist (by performing a biopsy)
  - Incisional vs. Excisional
  - Shave vs. Punch
- The more specimen a pathologist has the more likelihood of a diagnosis
- Excisional biopsy is generally preferred over incisional
  - However, there is no evidence in the literature that an incisional bx increases the risk of metastasis or affects the course of the disease
- Since depth determines staging and treatment, a punch would be preferable to shave for it will include fat and guide you in surgical therapy of the patient

Consultation

- Consultation with a specialist (pre- or post-biopsy)
  - Dermatologist (External Medicine)
  - Etc.
Differential Diagnosis

- **Melanocytic Nevus**
  - Junctional Nevus

- **Intradermal Nevus**
Differential Diagnosis

- Compound Nevus

Differential Diagnosis

- Melanocytic Nevus with Atypia or Dysplastic Nevus

Atypical Melanocytic Nevi

Dysplastic Nevus Syndrome
Differential Diagnosis

- Lentigo

Differential Diagnosis

- Ephelids (freckles)
Differential Diagnosis

- Blue Nevus

Differential Diagnosis

- Pigmented Basal Cell Carcinoma
Seborrheic Keratosis

Dermoscopy

Traumatic Tattoo
Staging

- T (Tumor Depth)
- N (Nodal Involvement)
- M (Metastasis)

Staging – cont’d

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumor (T)</th>
<th>Node (N)</th>
<th>Metastasis (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>is</td>
<td>NO</td>
<td>MO</td>
</tr>
<tr>
<td>IA</td>
<td>1a</td>
<td>NO</td>
<td>MO</td>
</tr>
<tr>
<td>IB</td>
<td>1b</td>
<td>NO</td>
<td>MO</td>
</tr>
<tr>
<td>2a</td>
<td></td>
<td>NO</td>
<td>MO</td>
</tr>
<tr>
<td>IIA</td>
<td>T2b</td>
<td>NO</td>
<td>MO</td>
</tr>
<tr>
<td>IIB</td>
<td>T3b</td>
<td>NO</td>
<td>MO</td>
</tr>
<tr>
<td>IIC</td>
<td>T4b</td>
<td>NO</td>
<td>MO</td>
</tr>
<tr>
<td>IIIA</td>
<td>T1-T4a</td>
<td>N1a or N2a</td>
<td>MO</td>
</tr>
<tr>
<td>IIIB</td>
<td>T1-T4b or T1-T4a/b</td>
<td>N1a, N1b, N2b or N2c</td>
<td>MO</td>
</tr>
<tr>
<td>IIIC</td>
<td>T1-T4a/b</td>
<td>N1b, N2b or N3</td>
<td>MO</td>
</tr>
<tr>
<td>IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1b/M1c</td>
</tr>
</tbody>
</table>

http://www.melanomacenter.org/staging/stages.html
## Tumor Thickness

<table>
<thead>
<tr>
<th>T0</th>
<th>Insitu (not penetrated the dermis)</th>
<th>a. without ulceration</th>
<th>b. with ulceration</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>&lt;1.0 mm</td>
<td>a. without ulceration</td>
<td>b. with ulceration</td>
</tr>
<tr>
<td>T2</td>
<td>1.01-2.0mm</td>
<td>a. without ulceration</td>
<td>b. with ulceration</td>
</tr>
<tr>
<td>T3</td>
<td>2.01-4.0mm</td>
<td>a. without ulceration</td>
<td>b. with ulceration</td>
</tr>
<tr>
<td>T4</td>
<td>&gt;4.01 mm</td>
<td>a. without ulceration</td>
<td>b. with ulceration</td>
</tr>
</tbody>
</table>

## Number of Nodes Involved

<table>
<thead>
<tr>
<th>No</th>
<th>0</th>
<th>a. micrometastasis</th>
<th>b. macrometastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1</td>
<td>1</td>
<td>a. micrometastasis</td>
<td>b. macrometastasis</td>
</tr>
<tr>
<td>N2</td>
<td>2-3</td>
<td>a. micrometastasis</td>
<td>b. macrometastasis</td>
</tr>
<tr>
<td>N3</td>
<td>4 or more</td>
<td>a. micrometastasis</td>
<td>b. macrometastasis</td>
</tr>
</tbody>
</table>
Site Location for Metastases

<table>
<thead>
<tr>
<th>M1a</th>
<th>Distant skin, subcutaneous and/or nodal involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1b</td>
<td>Lung Metastases</td>
</tr>
<tr>
<td>M1c</td>
<td>All other visceral metastases or any other distant mets</td>
</tr>
</tbody>
</table>

Sentinel Node Biopsy

- **Definition**
  - Location with a radio-opaque dye of closest node to the malignant lesion and removal of that node for microscopic examination
- **Melanomas of greater than 1.0 mm in depth histologically generally require sentinel node biopsy**
- **Controversy in the Dermatology Literature**
- **Controversy over staging vs. means of treatment**
- **Most authorities will agree that removal of a sentinel node does not adversely or positively affect the course of the disease. The patient’s outcome remains unchanged whether a sentinel node biopsy is performed**
- **Its values lies in staging the disease**
Clark’s Level of Depth of Invasion
For Tumor Thickness

Level 1 - Melanoma confined to epidermis
Level 2 - Melanoma invaded sparsely into the top layer of the papillary dermis
Level 3 - Melanoma invasion into the papillary dermis extensively
Level 4 - Invasion into deeper lower dermis the reticular dermis
Level 5 - Invasion into the subcutaneous fat
### Treatment

<table>
<thead>
<tr>
<th>T1</th>
<th>In situ</th>
<th>Simple excision with 5mm border</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1mm-1.0mm</td>
<td>Simple excision with 10mm border</td>
<td></td>
</tr>
<tr>
<td>1.1mm-2.0mm</td>
<td>Simple excision with 10-20mm border with sentinel node biopsy</td>
<td></td>
</tr>
<tr>
<td>2.1mm-4.0mm</td>
<td>Simple excision or graft or flap 20mm border and sentinel node bx</td>
<td></td>
</tr>
<tr>
<td>&gt;4.0mm</td>
<td>20-30mm excision with graft or flap and sentinel node biopsy</td>
<td></td>
</tr>
</tbody>
</table>

- Protocols for nodal or metastatic lesions require referral to an oncologist
- As a dermatologist I routinely refer patients with >1.1 mm lesions in depth to a general surgeon for sentinel node or more complete nodal evaluation
- Most surgeons will perform the appropriate excision at the time of nodal resection

- Since it’s unlikely as primary care physicians that you are going to perform node biopsies and consequently larger excisions, you’re most likely to refer all lesions greater than 1.0 mm in depth
- Your options may include referral on clinical suspicions or referral on pathological diagnosis for appropriate treatment
- Controlled microscopic excision is not of benefit when excising melanoma
  - Neither frozen sections or MOHS chemosurgery can adequately demonstrate malignant cells
**Advanced Metastatic Melanoma**

- **Melanoma Vaccine**
  - Metastatic disease without lung involvement has increased survival rates by 50% in patients receiving melanoma vaccine
  - A vaccine of patient’s own melanoma cells is prepared and boosts significantly the body’s own immune response
  - Longevity increased from approximately 12 months survival to 20 months

- **Pegylated Interferon Alfa-2B and High dose Interferon**
  - Both have slight benefit for advanced metastatic disease but invariably have significant side effects requiring discontinuance in over 35% of patients

- **Chemotherapy/Oncologist**

**Five Year Survival Rates by Lesion Thickness**

<table>
<thead>
<tr>
<th>Lesion Thickness</th>
<th>Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>&gt;98%</td>
</tr>
<tr>
<td>T1</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>T2a</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>T2b</td>
<td>80%</td>
</tr>
<tr>
<td>T3a</td>
<td>75%</td>
</tr>
<tr>
<td>T3b</td>
<td>60%</td>
</tr>
<tr>
<td>T4a</td>
<td>70%</td>
</tr>
<tr>
<td>T4b</td>
<td>40%</td>
</tr>
</tbody>
</table>

Clinical or microscopic Ulceration reduces survival rates approximately by 5% per tumor depth
Five Year Survival Rates

- **Nodal Involvement**
  - 40% survival with any node involvement
- **Metastasis**
  - 10% survival rate

Summary

*Location is to real estate as suspicion is to diagnosis in medicine. So what really counts in life for the realtor is location, location, location and for us practitioners is suspicion, suspicion, suspicion!*

- **Suspicion** ➔ **Diagnosis** ➔ **Treatment**
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